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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,282	01/30/2004	Arthur M. Krieg	C1039.70048US01	6192

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	**PAPER NUMBER**
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,282	KRIEG ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-39* is/are pending in the application.

4a) Of the above claim(s) *22-24 and 31-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21,25-30 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22-24 and 31-38* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 3
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 19-21, 25-30 and 39, species SEQ ID NO: 10, in the reply filed on October 30, 2006 is acknowledged. The traversal is on the ground(s) that a search and examination on the generic claim would not constitute an undue burden, particularly since specific SEQ ID Nos are not recited in the claims. It is noted that the generic oligonucleotide (as recited in claim 19) and SEQ ID NO: 10 will be examined in this application.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 22-24 and 31-38 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 30, 2006.

3. Claims 19-21, 25-30 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite the phrase, "delivery complex is less than 10 μm in size". However, there is no support in the instant specification for this limitation/element of the instant claims. Applicants' have asserted that the listed delivery complexes (sterols, cationic lipid, liposomes and virosomes) are believed to be known in the art to include complexes less than 10 μm in size (see

preliminary amendment remarks of 1/30/04). However, microcarrier delivery complexes have various sizes as evidenced by the state of the art. Caplan et al (US 2001/0031262) teaches that delivery complexes (liposomes, mircoparticles, microcarriers) vary in diameter size, see [0049] and [0062]. Chonn et al (Advanced Drug Delivery Reviews, 1998, 30:73-83) teaches liposomal drug delivery systems have a size distribution averaging less the 100 nm in diameter, see abstract. Polozova et al (BBA, 1997, 1326:213-224) teaches that liposomes having a size of 150-230 nm in diameter and other sizes such as >400 nm and 150-250 nm, see abstract and conclusion. Gregoriadis (TIBTECH, 1995, 13:527-537) teach that liposomes (i.e. delivery complexes) can vary in size from about 25-100nm to several microns in diameter (see figure 1, p. 528 and Table 1, pp 532-531). Further, Applicants do not indicate that the specification, via examples or references cited in the specification, chow that it is known in the art to include complexes less than 10 μm in size.

Therefore, an interference cannot be declared, as requested by Applicants in the preliminary amendment remarks of 1/30/04).

Further, the effective filing date for the pending claims is January 30, 2004, which is the first time the claimed invention (an immunostimulatory oligonucleotide/delivery complex, comprising an oligonucleotide linked to a biodegradable delivery complex, wherein the oligonucleotide comprises the sequence 5'-C, G-3', wherein said delivery complex is less than 10 μm in size) was disclosed.

4. Claims 19-21, 25-27, 30 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The

claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The pending claims are directed to an immunostimulatory oligonucleotide/delivery complex comprising an oligonucleotide linked to a biodegradable delivery complex, wherein the oligonucleotide comprises the sequence 5'-C, G-3', wherein said delivery complex is less than 10 μm in size.

A review of the specification discloses a list of immunostimulatory nucleic acids that could be used in the claimed invention. The claims, claim 19 for example, only provide that the immunostimulatory nucleic acid has 2 nucleotides (C and G). However, the specification does not teach an immunostimulatory oligonucleotide having only 2 nucleic acids, 5'-C, G-3' in the claimed immunostimulatory oligonucleotide/delivery complex. Further, there is no written description of a delivery complex less than 10 μm in size.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry,, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision

of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of immunostimulatory oligonucleotide/delivery complexes and compositions, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of compositions, the skilled artisan could not immediately recognize or distinguish members of the claimed antigenic compositions. In view of the above, the instant specification fails to meet the written description requirement as set forth under 35 U.S.C. 112, first paragraph.

A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original);

Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

A specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose. Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998). See also UMC Elecs. Co. v. United States, 816 F.2d 647, 652, 2 USPQ2d 1465, 1468 (Fed. Cir. 1987) ("[T]here cannot be a reduction to practice of the invention without a physical embodiment which includes all limitations of the claim."); Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d 588, 593, 44 USPQ2d 1610, 1614 (Fed. Cir. 1997) ("[A] reduction to practice does not occur until the inventor has determined that the invention will work for its intended purpose."); Mahurkar v. C.R. Bard, Inc., 79 F.3d 1572, 1578, 38 USPQ2d 1288, 1291 (Fed. Cir. 1996) (determining that the invention will work for its intended purpose may require testing depending on the character of the invention and the problem it solves).

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. >As

explained by the Federal Circuit, "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." Falkner v. Inglis, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). See also Capon v. Eshhar, 418 F.3d at 1358, 76 USPQ2d at 1084 ("The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes" where the genes were novel combinations of known DNA segments.).< For example, disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. Noelle v. Lederman, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described). Additionally, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. See Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene

does, rather than what it is." Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. See also Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.").

It is noted that Applicants have claimed a large genus of CpG immunostimulatory nucleic acids with only the C and G being defined in the oligonucleotide. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant

was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)(Claims directed to PTFE dental floss with a friction-enhancing coating were not supported by a disclosure of a microcrystalline wax coating where there was no evidence in the disclosure or anywhere else in the record showing applicant conveyed that any other coating was suitable for a PTFE dental floss.) On the other hand, there may be situations where one species adequately supports a genus. See, e.g., Rasmussen, 650 F.2d at 1214, 211 USPQ at 326-27 (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim

to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered); In re Herschler, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."); In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973) (the phrase "air or other gas which is inert to the liquid" was sufficient to support a claim to "inert fluid media" because the description of the properties and functions of the air or other gas segmentizing medium would suggest to a person skilled in the art that appellant's invention includes the use of "inert fluid" broadly.).

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 19-21, 25-30 and 39 are rejected under 35 U.S.C. 102(a) as being anticipated by Van Nest et al (US 2003/0129251; published July 10, 2003).

Van Nest et al discloses an immunostimulatory oligonucleotide/microcarrier complex and that the oligonucleotide is bound (i.e. linked) to a biodegradable

microcarrier (abstract). Van Nest et al discloses that the immunostimulatory oligonucleotide "...can be of any length greater than 6 bases or base pairs and generally comprises the sequence 5'-cytosine, guanine-3', preferably greater than 15 bases or base pairs, more preferably greater than 20 bases or base pairs in length. As is well-known in the art, the cytosine of the 5'-cytosine, guanine-3' sequence is unmethylated. An ISS may also comprise the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3'. An ISS may also comprise the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, C-3'. As indicated in polynucleotide sequences below, an ISS may comprise (i.e., contain one or more of) the sequence 5'-T, C, G-3'. In some embodiments, an ISS may comprise the sequence 5'-C, G, pyrimidine, pyrimidine, C, G-3' (such as 5'-CGTTCG-3'). In some embodiments, an ISS may comprise the sequence 5'-C, G, pyrimidine, pyrimidine, C, G, purine, purine-3'. In some embodiments, an ISS comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine-3' (such as 5'-AACGTT-3')." (see [0071]; [0153]) Van Nest et al discloses that the oligonucleotide is linked, covalently or non-covalently, to the biodegradable microcarrier in the complex (see [0014]; [0025]; [0026]). "We have discovered new compositions and methods for modulating immune responses in individuals, particularly humans. The compositions of the invention comprise an immunomodulatory polynucleotide (IMP) complexed with a biodegradable microcarrier (MC). We have found that immunomodulatory polynucleotides combined with nanometer-scale microcarriers (50 and 200 nm diameter beads) efficiently modulate immune cells, including human cells. IMPs combined with small microcarriers (approximately 1 to 4.5 μm, less than 2.0 μm or about 1.5 μm diameter) also immunomodulated human cells." (see [0020]; [0036]) Van Nest et al discloses that the "...complexes may include or

exclude an antigen. In some embodiments, the invention provides compositions comprising antigen-free IMP/MC complexes, i.e., IMP/MC complexes not linked to an antigen (directly or indirectly). In other embodiments, the invention provides compositions comprising IMP/MC complexes mixed with one or more antigens. In other embodiments, the invention provides compositions comprising IMP/MC complexes linked to antigen." (see [0022]) Van Nest et al discloses that the antigen can be an allergen (see [0049]).

Van Nest et al discloses that the "...complex can be administered in combination with other pharmaceutical and/or immunogenic and/or immunostimulatory agents and can be combined with a physiologically acceptable carrier thereof." (see [0151]) It is noted that the specification defines a pharmaceutically acceptable carrier to include "...substances that can be coadministered with a nucleic acid or a nucleic acid delivery complex and allows the nucleic acid to perform its indicated function. Examples of such carriers include solutions, solvents, dispersion media, delay agents, emulsions and the like. The use of such media for pharmaceutically active substances are well known in the art. Any other conventional carrier suitable for use with the nucleic acids falls within the scope of the instant invention." (see p. 43 specification)

The prior art anticipates the claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' complexes and compositions with the complexes and compositions of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed complexes and compositions and the complexes and compositions of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 19-21, 25-30 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al (WO 98/55495).

Schwartz et al discloses a complex that comprises an oligonucleotide in conjunction with an immunostimulatory peptide or antigen (abstract; p. 4). The prior art discloses that the complex can also comprise an encapsulating agent that can maintain the ISS and antigen (pp. 7-8; p. 13). Schwartz et al discloses that the oligonucleotides (i.e. ISS or IMP) comprise phosphorothioate backbones, which are phosphate backbone modifications (p. 11; p. 29). Schwartz et al discloses that the oligonucleotide can be combined with immunomodulatory facilitators such as adjuvants, such adjuvants include emulsions and polylactide/polyglycolide microparticles (i.e. microcarrier or delivery complex (p. 12, 14; claims). Schwartz et al discloses that the ISS can be covalently or non-covalently linked to the immunomodulatory facilitator (i.e. microcarrier or delivery complex) (p. 14). Schwartz et al discloses the size of the microcarrier or microparticle (see pp. 15-16). The size range is from about 0.04 μm to about 100 μm or from about 0.15 μm to about 10 μm (see p. 16).

The prior art discloses the claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' complexes and compositions with the complexes and compositions of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed complexes and compositions and the complexes and compositions of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 19-21, 25-27, 30 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al (Microbiol. Immunol., 1994, 38/10:831-836) or Sonehara et al (J. Interferon and Cytokine Research, 1996, 16:799-803), Cryz et al (European Commission Cost/STD Initiative, May 1996, pp. 665-690) taken with Tice et al, (5075109).

Yamamoto et al, for example, teaches a synthetic 22-mer oligonucleotide, comprising a 5'-C, G-3', and that this oligonucleotide has immunostimulatory activity (abstract; p. 831). Yamamoto et al teaches that the oligonucleotide is associated with a liposome (i.e. biodegradable delivery complex) (p. 832).

Cryz et al teaches biodegradable delivery complexes (i.e. liposomes) and that "liposomes are microspheres consisting of one or more lipid bilayers alternating with aqueous spaces. Their size varies from a minimum of about 30 nm to several microns. The main component of liposomes is an amphiphile (with hydrophobic and hydrophilic moieties), usually a phospholipid of which the acyl chains form the hydrophobic region of liposomes, with the polar group facing the water phase. Depending on the liquid-crystalline phase transition temperature (Tc) of the phospholipid, bilayers can be "fluid" or "rigid" at ambient temperature. Bilayer fluidity or rigidity can be altered by the addition of cholesterol and other sterols into the bilayer structure of liposomes." (p. 671, left column) Cryz et al also teaches that "the remarkable versatility of liposomes in terms of structural characteristics (e.g. vesicle size, surface charge, lipid composition), mode of antigen localization within the vesicles (e.g. entrapped, intercalated in the lipid bilayer, adsorbed on or covalently coupled to the vesicle surface) and the variety of route options for oral or parenteral administration, has allowed the design of numerous versions of the system for effective action on a variety of animal

species." (p. 671 right column) Yamamoto et al and Cryz et al teach the claimed immunostimulatory oligonucleotide/delivery complex except for the delivery complex being less that 10 μm in size.

However, Tice teaches delivering bioactive agents in a biocompatible excipient (i.e. biodegradable) to form microcapsules having a size ranging from between 1 micrometer to approximately 10 micrometers and administering this composition (abstract). Tice et al teaches that the bioactive agent or ingredient can be nucleic acids (col. 3, l. 45-60). Tice et al also teaches that the bioactive agent (i.e. nucleic acids) and delivery complex can be prepared for immunization in filtered sterilized tap water and sodium bicarbonate (col. 5, l. 53-56). Therefore it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Yamamoto et al, Cryz et al and Tice et al prepare a immunostimulatory oligonucleotide/delivery complex comprising an oligonucleotide linked to a biodegradable delivery complex, wherein the oligonucleotide comprises the sequence 5'-C, G-3', wherein said delivery complex is less than 10 μm in size. Both Yamamoto et al and Tice et al teach that oligonucleotides (i.e. nucleic acids) can be bioactive agents or have immunostimulatory activity. All three references teach the use of lipids or liposomes as carriers or biodegradable delivery complexes for bioactive agents (i.e. oligonucleotides or antigens). Tice et al teaches a particular delivery complex size to accommodate immunization. Cryz et al teaches that liposomes have the ability to as a potent immunological agent and that they can be used carriers or delivery complexes in vaccines and that because of the remarkable versatility of liposomes in terms of structural characteristics (e.g. vesicle size, surface charge, lipid composition), mode of antigen or oligonucleotide localization within the vesicles

(e.g. entrapped, intercalated in the lipid bilayer, adsorbed on or covalently coupled to the vesicle surface) and the variety of route options for oral or parenteral administration, has allowed the design of numerous versions of the system for effective action on a variety of animal species. In view of the combined teachings, one of skill in the art, at the time the invention was made, would have had a reasonable expectation of success of preparing the claimed invention from the prior art references. The claimed invention is prima facie obvious in view of the combined teachings of Yamamoto et al, Cryz et al taken with Tice et al, absent any convincing evidence to the contrary.

12. No claims are allowed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
March 13, 2007

FORM PTO-1449 A and B (modified PTO/SB/08)

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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APPLICATION NO.:	10/769,282	ATTY. DOCKET NO.:	C1039.70048US01
FILING DATE:	January 30, 2004	CONFIRMATION NO.:	6192
APPLICANT:	Krieg et al.		
GROUP ART UNIT:	1645	EXAMINER:	Nita M. Minnifield

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document Number	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
/NMM/	A1	4,452,775		Kent	06-05-1984
	A2	5,595,756		Bally et al.	01-21-1997
	A3	5,663,153		Hutcherson et al.	09-02-1997
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	A7	5,785,992		Ansell et al.	07-28-1998
	A8	5,849,719		Carson et al.	12-15-1998
	A9	5,965,542		Wasan et al.	10-12-1999
	A10	5,976,567		Wheeler et al.	11-02-1999
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	A19	6,214,806	B1	Krieg et al	04-10-2001
	A20	6,218,371	B1	Krieg et al.	04-17-2001
	A21	6,221,882		Macfarlane	04-24-2001
	A22	6,239,116	B1	Krieg et al.	05-29-2001
	A23	6,339,068	B1	Krieg et al.	01-15-2002
	A24	6,339,630		Macfarlane	06-04-2002
	A25	6,248,720	B1	Mathiowitz et al.	06-19-2001
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	A27	6,426,336	B1	Carson et al.	07-30-2002
	A28	6,429,199	B1	Krieg et al.	08-06-2002
	A29	6,479,504		Macfarlane et al.	11-12-2002
	A30	6,498,148	B1	Raz	12-24-2002
	A31	6,514,948	B1	Raz et al.	02-04-2003
	A32	6,521,637		Macfarlane	02-18-2003
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FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 10/769,282	ATTY. DOCKET NO.: C1039.70048US01
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Sheet 2 of 13	GROUP ART UNIT: 1645	EXAMINER: Nita M. Minnifield

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	A35	6,610,308		Haensler	08-26-2003
	A36	6,610,661	B1	Carson et al.	08-26-2003
	A37	6,630,455	B1	Mitchell	10-07-2003
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	A43	6,943,240		Bauer et al.	09-13-2005
	A44	6,949,520		Hartmann et al.	09-27-2005
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	A46	7,001,890		Wagner et al.	02-26-2006
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	A48	2002-0086839	A1	Raz et al.	07-04-2002
	A49	2002-0091097	A1	Bratzler et al.	07-11-2002
	A50	2002-0164341	A1	Davis et al.	11-07-2002
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Sheet 3 of 13	GROUP ART UNIT: 1645	EXAMINER: Nita M. Minnifield

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		A119	2004-0235774	A1	Bratzler et al.	11-25-2004
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		A122	2004-0247662	A1	Dow et al.	12-09-2004
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		A128	2005-0009774	A1	Krieg et al.	01-13-2005
		A129	2005-0013812	A1	Dow et al.	01-20-2005
		A130	2005-0032734	A1	Davis et al.	02-10-2005
		A131	2005-0032736	A1	Krieg et al.	02-10-2005
		A132	2005-0037403	A1	Krieg et al.	02-17-2005
		A133	2005-0037985	A1	Krieg et al.	02-17-2005
		A134	2005-0043529	A1	Davis et al.	02-24-2005
		A135	2005-0049215	A1	Krieg et al.	03-03-2005
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		A137	2005-0054601	A1	Wagner et al.	03-10-2005
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	A143	2005-0075302	A1	Hutcherson et al.	04-07-2005
	A144	2005-0176672	A1	Scheule et al.	08-11-2005
	A145	2005-0191342	A1	Tam et al.	09-01-2005
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	A149	2005-0119273	A1	Lipford et al.	06-02-2005
	A150	2005-0123523	A1	Krieg et al.	06-09-2005
	A151	2005-0130911	A1	Uhlmann et al.	06-16-2005
	A152	2005-0148537	A1	Krieg et al.	07-07-2005
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	A158	2005-0214355		Klinman et al.	09-29-2005
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	A161	2005-0233995	A1	Krieg et al.	10-20-2005
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	A170	2005-0249794	A1	Semple et al.	11-10-2005
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	A173	2005-0267057	A1	Krieg	12-01-2005
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Examiner's Initials #	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
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	B2	EP	0 468 520	A2	Mitsui Toatsu Chemicals, Inc.	01-29-1992	
	B3	WO	95/24929	A2	Brown University Research Foundation	09-21-1995	
	B4	WO	96/02555	A1	University of Iowa Research Foundation	02-01-1996	
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	B6	WO	97/30731	A3	The Immune Response Corporation	08-28-1997	
	B7	WO	97/42975	A2	Genemedicine Inc.	11-20-1997	
	B8	WO	98/29557	A1	Biovector Therapeutics	07-09-1998	Y-Abstract
	B9	WO	98/51278	A2	INEX Pharmaceuticals Corp.	11-19-1998	
	B10	WO	99/30686	A1	INEX Pharmaceuticals Corporation	06-24-1999	
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	B14	WO	00/03683	A2	INEX Pharmaceuticals Corporation	01-27-2000	
	B15	WO	00/06588	A1	University of Iowa Research Foundation	02-10-2000	
	B16	WO	00/15256	A2	Pasteur Merieux Serums Et Vaccins [FR]	03-23-2000	Y-Abstract
	B17	WO	00/20039	A1	The Regents of the University of California	04-13-2000	
	B18	WO	00/45849	A2	Genzyme Corporation	08-10-2000	
	B19	WO	00/46365	A1	Virginia Commonwealth University	08-10-2000	
	B20	WO	01/35991	A2	Dynavax Technologies Corporation	05-25-2001	
	B21	WO	01/68143	A2	Dynavax Technologies Corporation	09-20-2001	
	B22	WO	01/68144	A2	Dynavax Technologies Corporation	09-20-2001	
	B23	WO	02/28428	A2	Aventis Pasteur [FR]	04-11-2002	Y-Abstract
	B24	WO	03/000232	A2	Dynavax Technologies Corporation	01-03-2003	
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	B28	WO	2004/007743	A2	Coley Pharmaceutical GmbH	01-22-2004	
	B29	WO	2004/014322	A2	Dynavax Technologies Corp.	02-19-2004	
	B30	WO	2004/026888	A2	Coley Pharmaceutical GmbH	04-01-2004	
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